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In the specification, insert the paragraph below on a separate page at the end of the application:

**ENHANCEMENT OF ADENOVIRAL ONCOLYTIC ACTIVITY IN PROSTATE CELLS  
BY MODIFICATION OF THE E1A GENE PRODUCT**

**Abstract of the Disclosure**

The present invention relates to compositions and methods for enhancing the oncolytic activity of replication-competent, target cell-specific adenovirus vectors by modification of the E1A gene product. The target cell-specific replication-competent adenovirus vectors comprise a chimera of an adenovirus gene essential for replication, preferably an early gene, and the Androgen receptor (or a portion thereof) under the transcriptional control of a cell type-specific transcriptional regulatory element (TRE). By providing for cell type-specific transcription through the use of one or more cell type-specific TREs, the adenovirus vectors effect prostate-specific cytotoxicity due to selective replication.

In the specification, please relace the paragraph on page 48 beginning at line 8 and ending on page 49, with the following paragraph:

**Plasmid Construction.** E1A fragment was synthesized (approximately 1 kb) from the wild type adenovirus type 5 by PCR using the primer pair of 5'-TCACTCGGATCCACCGGGACTGAAAATGAGACATAT (SID NO: 14) and 5'-TACATCACTC GCGGCCGCTGGCCTGGGGCGTTTACAGCTCA (SID NO: 15). This E1A product was cloned into the vector pCR2.1.-TOPO (Invitrogen) to generate TOPO-E1A plasmid, in which the E1A sequence was verified by sequencing analysis. Full-length of androgen receptor (AR full-length), AR without ligand-binding domain (AR ORF 1-1959 bps, named AR TAD-DBD), and AR DNA-binding domain alone (AR ORF 1669-1959 bps, named AR DBD) were synthesized from the AR cDNA by PCR using the primer pairs of 5' TACATCACTCGCGGCCGCGAGAAGTGCAGTTAGGGCTGGGAA (SID NO: 16) and 5'-TCAC TCCTCGAGTC ACTGGGTGTGGAAATAGATGGGC TT

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(SID NO: 17) for AR full-length (approx. 2.7 kb), 5'-TACATCACTCGCGGCCGCAGAAAGTGCAGTTAGGGCTGGG AA(SID NO: 18) and 5'-TCACTCCTC GAGTCACTCAGTGGGGCT GGTGGT GCTGGA (SID NO: 19) for AR-TAD-DBD (approx. 2 kb), 5'-TACATCACTCGCGGCCGCAAAGACCTGCCTGATCTGTGGAGAT (SID NO: 20) and 5'-TCACTCCTC GAGTCACTCAGTGGGGCT GGTGGT GCTGGA (SID NO: 19) for AR-DBD (approx. 320 bps). These three different lengths of AR PCR products were cloned into the vector pCR2.1-TOPO to generate the plasmids of TOPO-AR full-length, TOPO-AR TAD-DBD, TOPO-AR DBD, in which the sequence of these AR inserts were verified by sequencing analysis. The AR fragments were cleaved from TOPO-AR by Not I and Xho I restriction enzyme digestion and inserted at the downstream of the TOPO-E1A to create TOPO-E1A-AR. The E1A-AR fragments were cleaved from TOPO-E1A-AR plasmids by BamH I and Xho I and cloned into pBK-CMV to create the pBK-CMV/E1A-AR constructs. The E1A fragment was cloned into pBK-CMV to create the pBK-CMV/E1A construct. For cloning of E1A reporter plasmid pE1B-luc, E1B promoter with Hind III and BamH I ends was synthesized from Ad5 wild type virus by PCR amplification using primer pair 5'-CCCAAGCTTTCCTTCTAACACACCTCCTG (SID NO: 21) and 5'-CGGGATCCGA GGTCAGATGTAACCAAGA (SID NO: 22). The Luciferase gene was cleaved from the plasmid pBK-PSE-PBN-Luc with BamHI and XmaI. The PCR product of E1B promoter and the Gel purified luciferase were cloned into the pUC 19 vector with ends of Hind III and Xma I, generating the E1A reporter plasmid pE1B-luc. The plasmid pcDNA3-hAR was a kindly gift from Dr. William Isaacs. To construct the plasmids that the E1A-AR gene expressions are under the control by the prostate specific enhancer (PSE) and rat probasin promoter (PBN), the prostate specific reporter plasmid pBK-PSE-PBN-luc was digested with BamHI and XhoI to remove the luciferase gene. The large fragments containing pBK-PSE-PBN were gel-purified and ligated with the BglII-XhoI fragments of E1A-AR inserts cleaved from pBK-CMV/E1A-AR, generating the plasmids pBK-PSE-PBN-E1A-AR. The E1A-AR chimera in the pBK-PSE-PBN-E1A-AR plasmids includes wild type AR (E1A-AR), transactivation domain of AR (E1A-TAD), and a full-length AR with a point mutation C685Y in the ligand binding domain (E1A-AR.sup.C685Y). The plasmid pBK-PSE-PBN-E1A was constructed by replacing the luciferase gene in the plasmid pBK-PSE-PBN-luc with E1A

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fragment. All PCR-derived fragments and site-directed mutagenesis were sequenced to confirm their predicted composition.

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